

Appl. No.: 10/750,076  
Amdt. dated February 5, 2007  
Reply to Office Action of October 5, 2006

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Amendments to the Claims:

1. (Original) A method for preparing an injectable formulation of interferon-beta (IFN- $\beta$ ) comprising:
  - a) preparing a first solution comprising IFN- $\beta$ , isolating a pool of purified IFN- $\beta$  from this solution, and precipitating said IFN- $\beta$  from this pool using an alcohol to form a precipitate;
  - b) dissolving said precipitate in guanidine hydrochloride (HCl) to form a second solution comprising resolubilized denatured IFN- $\beta$  and guanidine HCl;
  - c) diluting said second solution into a first buffer to obtain a third solution comprising resolubilized renatured IFN-beta and residual guanidine HCl; and
  - d) removing residual guanidine HCl from said third solution by diafiltration or dialysis of said third solution into a second buffer that is pharmaceutically acceptable, whereby said injectable formulation of IFN- $\beta$  is prepared.
2. (Original) The method of claim 1, wherein said second buffer contains arginine or sodium chloride.
3. (Original) The method of claim 1, wherein said first buffer has a pH of about 5.0 to about 8.0, and wherein said residual guanidine HCl is present in said third solution at a concentration of 1.6 M or less.
4. (Original) The method of claim 1, wherein said IFN- $\beta$  has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.
5. (Currently Amended) The method of claim 1, wherein said IFN- $\beta$  is glycosylated ~~or unglycosylated~~.

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6. (Original) The method of claim 1, wherein said IFN- $\beta$  is recombinantly produced.

7. (Currently Amended) The method of claim 1, wherein said IFN- $\beta$  has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program (version 2.0) with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

8. (Original) A method for preparing an injectable formulation of interferon-beta (IFN- $\beta$ ), said method comprising denaturation of IFN- $\beta$  with guanidine hydrochloride (HCl) followed by renaturation of the IFN- $\beta$  via dilution into a first buffer to obtain a renatured IFN- $\beta$  solution comprising residual guanidine HCl, and removing said residual guanidine HCl from said renatured IFN- $\beta$  solution by diafiltration or dialysis of said renatured IFN- $\beta$  solution into a second buffer that is pharmaceutically acceptable, whereby said injectable formulation of IFN- $\beta$  is prepared.

9. (Original) The method of claim 8, wherein said first buffer has a pH of about 3.0 to about 5.0, and wherein said residual guanidine HCl is present in said renatured IFN- $\beta$  solution at a concentration of 1.6 M or less.

10. (Original) The method of claim 9, wherein said first buffer has a pH of about 3.0 to about 4.0, and wherein said residual guanidine HCl is present in said renatured IFN- $\beta$  solution at a concentration of 0.2 M or less.

11. (Original) The method of claim 10, wherein said first buffer has a pH of about 3.0, and wherein said residual guanidine HCl is present in said renatured IFN- $\beta$  solution at a concentration of 0.1 M or less.

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12. (Original) The method of claim 8, wherein said IFN- $\beta$  has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

13. (Currently Amended) The method of claim 8, wherein said IFN- $\beta$  is glycosylated ~~or unglycosylated~~.

14. (Original) The method of claim 8, wherein said IFN- $\beta$  is recombinantly produced.

15. (Currently Amended) The method of claim 8, wherein said IFN- $\beta$  has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program (version 2.0) with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

16. (Original) A method for preparing a composition comprising substantially monomeric interferon-beta (IFN- $\beta$ ), said method comprising:

- a) preparing a precipitate of substantially purified IFN- $\beta$ ;
- b) dissolving said precipitate in guanidine hydrochloride (HCl) to obtain a first solution comprising resolubilized denatured IFN- $\beta$ ; and
- c) renaturing said IFN- $\beta$  by dilution of said first solution with a buffer solution.

17. (Original) The method of claim 16, wherein said buffer solution has a pH of about 5.0 to about 8.0.

18. (Original) The method of claim 16, wherein said IFN- $\beta$  has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

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19. (Currently Amended) The method of claim 16, wherein said IFN- $\beta$  is glycosylated ~~or unglycosylated~~.

20. (Original) The method of claim 16, wherein said IFN- $\beta$  is recombinantly produced.

21. (Currently Amended) The method of claim 16, wherein said IFN- $\beta$  has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program (version 2.0) with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

22. (Original) A method for preparing an injectable formulation of interferon-beta (IFN- $\beta$ ), said method comprising:

- a) obtaining a sample comprising substantially purified IFN- $\beta$ ;
- b) mixing said sample with guanidine hydrochloride (HCl) to obtain a first solution comprising solubilized denatured IFN- $\beta$ ;
- c) diluting said first solution into a first buffer to obtain a second solution comprising solubilized renatured IFN-beta and residual guanidine HCl; and
- d) removing residual guanidine HCl from said second solution by diafiltration or dialysis of said second solution into a second buffer that is pharmaceutically acceptable, whereby said injectable formulation of IFN- $\beta$  is prepared.

23. (Original) The method of claim 22, wherein said first buffer has a pI of about 3.0 to about 5.0, and wherein said residual guanidine HCl is present in said second solution at a concentration of 1.6 M or less.

24. (Original) The method of claim 23, wherein said first buffer has a pH of about 3.0 to about 4.0, and wherein said residual guanidine HCl is present in said second solution at a concentration of 0.2 M or less.

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25. (Original) The method of claim 24, wherein said first buffer has a pII of about 3.0, and wherein said residual guanidine HCl is present in said renatured IFN- $\beta$  solution at a concentration of 0.1 M or less.

26. (Original) The method of claim 22, wherein said IFN- $\beta$  has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

27. (Currently Amended) The method of claim 22, wherein said IFN- $\beta$  is glycosylated ~~or unglycosylated~~.

28. (Original) The method of claim 22, wherein said IFN- $\beta$  is recombinantly produced.

29. (Currently Amended) The method of claim 22, wherein said IFN- $\beta$  has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program (version 2.0) with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

30. (Original) A method for preparing a composition comprising substantially monomeric interferon-beta (IFN- $\beta$ ), said method comprising:

- a) preparing a sample comprising substantially purified IFN- $\beta$ ;
- b) mixing said sample with guanidine hydrochloride (HCl) to obtain a first solution comprising solubilized denatured IFN- $\beta$ ; and
- c) renaturing said IFN- $\beta$  by dilution of said first solution with a buffer solution.

31. (Original) The method of claim 30, wherein said buffer solution has a pII of about 3.0 to about 5.0.

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32. (Original) The method of claim 30, wherein said IFN- $\beta$  has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

33. (Currently Amended) The method of claim 30, wherein said IFN- $\beta$  is glycosylated ~~or unglycosylated~~.

34. (Original) The method of claim 30, wherein said IFN- $\beta$  is recombinantly produced.

35. (Currently Amended) The method of claim 30, wherein said IFN- $\beta$  has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program (version 2.0) with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.